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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
WALICKA, MALGORZATA A

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 07/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/647,780	OUIMET ET AL.	
	Examiner	Art Unit	
	Malgorzata A. Walicka	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 May 2003* .

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13,15 and 16* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,11,13,15 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *sequence alignment* .

Continuation of Disposition of Claims: Claims withdrawn from consideration are 1-6, 11, 13 and 15-16 in part concerning SEQ ID NO:2 and 7-10, and 12.

The Amendment filed on May 5, 2003, as paper No. 18 is acknowledged. The amendments to the specification and claims have been entered as requested. Claim 14 is cancelled; new claims 15 and 16 are entered. Claims 1-13 and 15-16 are pending in the application. Claims 1-6, 11, 13 and 15-16, in part concerning SEQ ID NO: 4, are the subject of this office action. Claims 1-6, 11, 13 and 15-16 in part concerning SEQ ID NO: 2, as well as claims 7-10 and 12 are withdrawn from examiner's consideration as directed to the non-elected invention.

DETAILED ACTION

1. Objection

In the previous Office Action, paper No.16, the specification has been objected to for a vague definition of the term "biologically active", "similar" and "metalloprotease activity". The objection is not withdrawn.

In the specification, on page 2, line 13, Applicants write: "biologically active, i.e. they have biological properties identical or similar of the biological properties of the NEP II polypeptide of SEQ ID NO. 2 or SEQ ID NO. 4, namely metalloprotease activity."

The term "similar" is a relative term, which renders the definition of the term "biologically active" indefinite. One of ordinary skill in the art would not be reasonably aprised of the scope of the term. It is unclear how similar the activity should be to be within the scope of the term "metalloprotease activity". In addition, the term "metalloprotease activity" itself has a very broad meaning, because there is a large number of metalloproteases. Therefore, it is not known which metalloprotease activity

Applicants mean, especially that any metalloprotease activity of SEQ ID NO: 4, or SEQ ID NO: 2, is disclosed in the application.

In their Response, in REMARKS, page 2, line 22, Applicants write:

> "With regard to the term 'metalloprotease activity', Applicants respectfully note that metalloproteases are enzymes having catalytic activity which involves a metallic ion. Accordingly, the one skilled in art can readily identify an enzymatic activity as being a metalloprotease activity using a chelatant agent such as EDTA (see e.g., Appendix A, extract of Roche Molecular Biochemicals, The Complete Guide for Protease Inhibition that describes $EDTANa_2$ as a specific inhibitor of metalloproteases)."

This argument of Applicants is not found persuasive, because nowhere in the specification Applicants mention that the activity of polypeptide of SEQ ID NO: 4 is inhibited by $EDTANa_2$, as Applicants do not disclose any substrate of said polypeptide, and because of that, any enzymatic reaction that can be inhibited by $EDTANa_2$. Furthermore, many enzymes that need metallic ions for their activity are inhibited by $EDTANa_2$. DNA polymerases are the classic example.

Further, Applicants write,

"To further evidence that one skilled in the art would readily recognize that NEP2 is a zincin, Applicants have attached an article from the inventors (Rose et al) that further supports

that the claimed NEP2 is a zincin, and more specifically a member of the M13 subfamily of metalloproteases" (page 3, line 11).

This argument of Applicants is found not persuasive. The examined claims are directed to SEQ ID NO: 4 that is a human sequence and the paper characterizes the rat NEP2.

Traversing objections to the term "similar" Applicants write on page 4, line 1:

> "With regard to the term 'similar', in context with the complete present disclosure, and in particular, the whole sentence, the term 'similar' has to be understood as referring to properties identical or similar to that of NEP2. In any event, said activity similar to that of NEP2 has to be a metalloprotease."

This argument of Applicants is found not persuasive. Firstly, when a thing is similar to the other thing, it is not identical. Secondly, the kind of enzymatic activity can only be the same or different. A polypeptide may be a metalloprotease or ligase. There is nothing like a ligase that is a little bit of metalloprotease or similar to metalloprotease.

In summary objection to the specification is not withdrawn.

2. Rejections

2.1. 35 USC section 101

Claims 1-2, 4-6, 11, 13, and new claims 15 and 16, are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility. The reasons are presented in the previous Office Action, paper No.16.

Traversing the examiner's position that annotation of protein function on the basis of homology to the protein with a well established biologic function is in many cases erroneous, as strikingly illustrated by the paper of Seffernick et al., Applicants state,

> "The Examiner has misinterpreted the teaching of Seffernick et al and drawn a general rule from a situation that is described by Seffernick et al. themselves as exceptional" (page 5).

Furthermore, Applicants pinpoint that the utility of the claimed NEP2 is further supported by the paper by Rose et al. and repeat that the HEXXH motif of zinc binding and homology between NEP2 and ECE/NEP/Kell enzymes support the utility as well.

The Applicant arguments have been fully considered, but are found not persuasive for the following reasons.

Those skilled in the art realize that annotating protein function on the basis of homology to the protein with a well established biologic function is in many cases erroneous even in one may be surprised by her own data. There are many reviews dealing with the problem; Applicants' attention is, for example, drawn to the paper by Devos et al. 2001, copy enclosed. The analysis performed by Devos et al. clearly indicates that in the case of three microbial genomes annotating cellular functions is

erroneous in more that 33% and annotating biding site is prone to even greater error; see table 1, page 430. One skilled in the art realizes that in case of mammalian and human genomes the percentage of error may be even higher due to complexity of mammalian genome expression, particularly due to splicing. In addition, those skilled in the art realize that even a single change in the amino acid sequence may inactivate that protein or change it biologic function.

As stated above in section *1. Objection,* the elected invention is human polypeptide of SEQ ID NO:4. The paper by Rose refers to rat NEP2; see INTRODUCTION, right column, and EXPERIMENTAL: " Total RNA from rat brain and testis ..." (the first line of section 'Expression of NEP2 splice variants in mammalian cell lines).

Applicants argue that the inventors' article (Rose at al) "supports that the claimed NEP2 is a zincin, and more specifically a member of the M13 subfamily of metalloproteases" (page 3 line 13). However, as indicated above, in objection to the specification, Rose at al. disclose a rat NEP2, which is not the polypeptide containing SEQ ID NO: 4 of human origin.

In summary, Applicants' assertion that a protein comprising SEQ ID NO: 4 is a novel human membrane-bound metalloprotease is increadable. Applicants have failed to establish any function or specific and substantial utility for the polypeptide of SEQ ID NO: 4, because the polypeptide is not disclosed to have any biologic activity.

Claims 1-6, 11, 13 and new claims 15-16 are rejected under 35 USC § 112, the first paragraph. Since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention, so that it would operate as intended, without undue experimentation.

Rejection of claim 6 for being directed to product of nature is withdrawn because the claim has been amended.

3.2. 35 USC section 112, second paragraph

Rejection of claims 1–2, 4-6, 11 and 13 are rejected under 35 U.S.C. 112, for indefinite terms:

1) a sequence derived from the sequence of SEQ ID NO: 4 or 3, and

2) a sequence homologous to the sequence of SEQ ID NO: 4 or 3,

is withdrawn because the claims have been amended.

Claims 1–2, 4-6, 11 and 13 and new claims 15-16 are still rejected because of the use of indefinite term "a biologically active" fragment of SEQ ID NO: 4.

The reasons are stated in the previous Office Action paper number 16 and reiterated herein. The term "biologically active" is defined on page 3, line 13, where Applicants write: "Said polypeptides derived from or homologous to, or the polypeptide fragments of, the polypeptide of sequence SEQ ID NO. 2 or SEQ ID NO. 4 are biologically active, i.e. they have biological properties identical or similar of the biological

properties of the NEP II polypeptide of SEQ ID NO. 2 or SEQ ID NO. 4, namely metalloprotease activity."

The term "similar" used in definition is a relative term, which renders the definition of the term "biologically active" indefinite. One of ordinary skill in the art would not be reasonably appraised of the scope of the term. It is unclear how similar the activity should be to be within the scope of the term "metalloprotease activity". In addition, the term "metalloprotease activity" itself has a very broad meaning, because there is a large number of metalloproteases. Therefore, it is not known which metalloprotease activity Applicants mean, especially that no specific metalloprotease activities of SEQ ID NO: 4, or SEQ ID NO: 2, are disclosed in the application.

Rejection of claim 3 as being indefinite for reciting the term "hybridize specifically" is withdrawn because the claim has been amended.

Rejection of claim 11 and 13 made under 35 U.S.C. 112, second paragraph as being incomplete for omitting essential steps in the claimed method is withdrawn because the claims have been amended.

3.3. 35 USC section 112, first paragraph

3.3.1. Lack of written description

Claims 1-2, 4-6, 11, 13 and new claims 14-16 are rejected under 35 U.S.C. 112, first paragraph for reasons stated in the previous Office Action. Amino acid sequence of SEQ ID NO: 4 consists of 116 amino acids, however its encoding SEQ ID NO: 3 consists of only 327 nucleotides. The nucleotide sequence encoding 116 amino acid

should be 348 nucleotides long. SEQ ID NO: 3 encodes residues 1-109 of SEQ ID NO: 4. Thus, the last 7 amino acids of the C-terminal of claimed human polypeptide are missing their codons. As such, the actual sequence of the polypeptide of SEQ ID NO: 4 is unclear.

Traversing this rejection Applicants write that SEQ ID NO: 4 is "a partial amino acid sequence of NEP2 in humans", and, "Since SEQ ID NO: 3 encodes only a portion of NEP2, and not necessarily the entire NEP2, let alone encoding the complete sequence of SEQ ID NO: 4 it is not inconsistent that SEQ ID NO: 3 has only 327 nucleotides rather than 348 nucleotides."

This argument of applicant is found not persuasive for the following reasons. Although SEQ ID NO: 4 and SEQ ID NO: 3 are not full length sequences, SEQ ID NO: 3 has to encode SEQ ID NO: 4, otherwise Applicants claim two inventions, and there is lack of unity of the elected Group VI comprising claim(s) 1-6, 11, 13 and new claims 15 and 16, drawn to novel membrane protease of SEQ ID NO: 4, encoding DNA, expression vector, host cell, antibody and a method of use the enzyme in screening for its inhibitors.

Claim 1, 6, 11, 13 and new claims 15-16 are rejected under 35 U.S.C. 112, first paragraph, for reasons stated in the previous Office Action and reiterated herein.

Claim 1, 6, 11. 13 and 15-16 are rejected as directed to polypeptides that comprise:

a) SEQ ID NO: 4,

b) a sequence 75% homologous to SEQ ID NO: 4or

c) a biologically active fragment of SEQ ID NO: 4.

The claims are directed to a large and variable genus of polypeptides. The specification discloses only a single species of the claimed genus, i.e., SEQ ID NO: 4. Although Applicants assure that this short 119 amino acid sequence is a metalloprotease, based on the fact that it contains the zinc binding motif, the disclosure does not present any longer polypeptide, which comprises SEQ ID NO: 4 and has the metalloprotease activity. The specification is silent about any structure/function relationship for SEQ ID NO: 4. Also, the specification does not teach any polypeptide whose structure is such that it contains the amino acid sequence that is in 75% identical to SEQ ID NO: 4 and has the metalloprotease activity. Thus, the structure and function of the other species of the genus are not disclosed, including the species listed under c). The Applicants have not provided information sufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filled.

Claims 2, 4 and 5 are rejected under 35 U.S.C. 112, for the reasons stated in the previous Office Action and reiterated herein.

The claims are directed to the large and variable genus of DNA molecules that comprise a sequence selected form the group of:

a) SEQ ID NO: 3,

b) a sequence that is in 75% is identical to SEQ ID NO: 3

c) a nucleotide sequence complementary to that of a) or b).

The claims are generic and lacking functional and structural description of claimed DNA molecules. The specification discloses only a single species of the claimed genus, i.e. SEQ ID NO: 3. However, the species is not disclosed as encoding the metalloprotease function, because the amino acid sequence that is supposed to be encoded by SEQ ID NO: 3 is not encoded by SEQ ID NO: 3. The structure and function of the other species of the claimed genus are not disclosed. Applicants do not teach the structure of any DNA molecule that comprises any of sequences a)-c) and has the desirable function to encode a metalloprotease. Therefore, the disclosure does not provide information sufficient to put one of skill in the art in possession of the attributes and features of species within the claimed genus. Thus, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filled.

In addition, new claims 15 and 16 are rejected, because of recitation by claim 15 "the peptide transmission in which NEP2 participates." The specification is silent as to in which peptide transmission SEQ ID NO: 4 is involved. Furthermore, with regards to claim 16 Applicants do not disclose any peptide transmission that is specifically related and/or disturbed in the group of diseases recited by the claim. Hence, because the disclosure does not provide information sufficient to put one of skill in the art in possession of the attributes and features of the peptide transmission in which the polypeptide of SEQ ID NO: 4 is involved, one skilled in the art cannot reasonably

conclude that the Applicant had possession of the claimed invention at the time the instant application was filled.

3.3.2. Scope of enablement

Assuming that 1) SEQ ID NO: 4 identifies a metalloprotease, and 2) SEQ ID NO: 3 encodes SEQ ID NO: 4 the following rejections are proper.

Claims 1, 6, 11, 13 and new claims 15, 16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polypeptide identified by SEQ ID NO: 4, does not reasonably provide enablement for all peptides that comprise

a) SEQ ID NO: 4,

b) a sequence identical to SEQ ID NO: 4 in 75%, and

c) a biologically active fragment of SEQ ID NO: 4.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. The genus of polypeptides listed under a) – c) is a large and variable genus lacking enabling description; see the above rejection for lack of written description.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Otherwise, undue experimentation is necessary to make the claimed invention. Factors to be considered in determining whether undue experimentation is required, are summarized *In re* Wands

[858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the nature of the invention, (b) the breadth of the claim, (c) the state of the prior art, (d) the relative skill of those in the art, (e) the predictability of the art, (f) the presence or absence of working example, (g) the amount of direction or guidance presented, (h) the quantity of experimentation necessary.

The nature and breath of the claimed invention encompasses any polypeptide comprising

a) SEQ ID NO: 4,

b) a sequence 75% homologous to SEQ ID NO: 4, and

d) a biologically active fragment of SEQ ID NO: 4.

The source of this polypeptide may be man-made or any living organism. While methods of gene cloning and manipulation are well known in the relevant art, and skills of the artisans highly developed, constructing this extremely large number of all possible DNA molecules encoding these polypeptides, expressing them, and checking enzymatic activity of expressed polypeptides is outside the realm of routine experimentation.

The disclosure does not set forth identifying characteristics of polypeptides listed under b) - c). Applicants did not provide any guidance as to the structure comprising SEQ ID NO: 4, for example, a full size enzyme or any other polypeptide comprising SEQ ID NO: 4. For the same reasons the specification is missing any instructions as to how to change the amino acid SEQ ID NO: 4 so that it was 75% identical to the initial sequenceand retained the desired activity. Even obtaining the biologically active fragment is not enabled because no fragment of SEQ ID NO: 4 is identified to be a

biologically active fragment. Without further guidance on the part of Applicants the experimentation left to those skilled in the art is improperly extensive and undue.

Claims 2 and 4-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the DNA identified by SEQ ID NO: 3, does not reasonably provide enablement for all the DNA molecules that

a) comprise SEQ ID NO: 3,

b) comprise a sequence that is 75% homologous to SEQ ID NO: 3

c) comprise a nucleotide sequence complementary to that of a) –c).

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. The genus of DNA molecules that comprise molecules enumerated under a) - c) is a large and variable genus encompassing the species that do not encode the protein having the desired functionality.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Otherwise, undue experimentation is necessary to make the claimed invention. Factors to be considered in determining whether undue experimentation is required, are summarized *In re* Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the nature of the invention, (b) the breadth of the claim, (c) the state of the prior art, (d) the relative skill of those in the art, (e) the predictability of the art, (f) the presence or

absence of working example, (g) the amount of direction or guidance presented, (h) the quantity of experimentation necessary.

The nature and breath of the claimed invention encompasses any isolated nucleic acid molecule that

a) comprise SEQ ID NO: 3,

b) comprise a sequence that is 75% homologous to SEQ ID NO: 3

c) comprise a nucleotide sequence complementary to that of a) –c).

The source of this molecule is man-made or any living organism. While methods of gene cloning and manipulation are well known in the relevant art, and skills of the artisans highly developed, isolating or constructing an extremely large number of all possible DNA molecules characterized under a)-c) is outside the realm of routine experimentation.

The disclosure does not set forth any identifying characteristics of the above listed DNA molecules. Applicants did not provide any guidance or examples what a DNA molecule that is at least 75% homologous to SEQ ID NO: 3 should be, so as to preserve the capacity of encoding the polypeptide with required functionality. Without that guidance the experimentation left to those skilled in the art is improperly extensive and undue.

3.4. 35 USC, 102

Rejection of claims 1 and 2 under 35 U.S.C. 102(b) as being anticipated by Shipp et al. is withdrawn, because the claims have been amended.

Claim 6 remains rejected under 35 U.S.C. 102(b) for the reasons stated in the previous Office Action, paper No 16 and reiterated herein. Claim 6 is rejected under 35 U.S.C. 102(b) as being anticipated by Shipp et al. (Molecular cloning of the common acute lymphoblastic leukemia antigen (CALLA) identifies type II integral membrane protein, Proc. Natl. Acad. Sci. USA, 1988, 85, 4819-4823, and Ritz et al. (A monoclonal antibody to human acute lymphoblastic leukaemia antigen; Nature 1980, 283; 583-585.

The amended claim 6 is directed to mono-or polyclonal isolated antibodies or their fragments, chimeric isolated antibodies or immunoconjugates, characterized in that they are obtained using a polypeptide and are capable of recognizing specifically a polypeptide comprising SEQ ID NO:4 or a sequence having at least 75% identity to SEQ ID NO:4 or a biologically active fragment of said sequence.

Shipp et al., page 4821, Fig. 2, teach a protein called CALLA antigen containing in positions 583-696 the amino acid sequence identical in 66.7% to amino acid residues 1-114 of SEQ ID NO: 4. Ritz et al. teach production of monoclonal antibody against CALLA. Ritz et al teach the invention of claim 6, because the antibody specific to the sequence that is 66.7% identical to SEQ ID NO: 4 will combine to the antibody specific to the sequence that is 66.7% identical to SEQ ID NO: 4 will combine to the sequence being 75% identical to SEQ ID NO:4.

In their "REMARKS" Applicants write, "antisera with CALLA specifically identify a single glycoprotein with a molecular weight of 95-100.00 (see Ritz et al. page 584, right column,

second paragraph, and Figure 1, line g), i.e. the CALLA protein." (page 11, line 3).

This argument of Applicants has been fully considered, but is found not persuasive. Applicants claim antibodies to polypeptides comprising SEQ ID NO:4. Polypeptides with molecular weight of 90-100 KDa are in the scope of the claim. Furthermore, an antibody specific to the polypeptide comprising sequence that is 66.7% identical to SEQ ID NO: 4 will combine to the polypeptide comprising the sequence being 75% identical to SEQ ID NO:4. Since the Office does not have a laboratory to test the reference by Ritz et al., it is Applicant's burden to show that the reference antibodies do not bind to a polypeptide comprising a polypeptide being 75% identical to SEQ ID NO: 4 as recited in the claim. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980).

New rejection

Claim 3 is rejected under 35 U.S.C. 102(b) as being anticipated by Bonaldo et al (Normalization and subtraction: two approaches to facilitate gene discovery, Genome Res. 1996, 6 (9), 791-809.

The claim is directed to a nucleotide sequence having a nucleotide sequence chosen from the sequences SEQ ID NOs: 5-27.

Bonaldo et al. disclose nucleotide sequences comprising, i.e. having SEQ ID NO: 15 and SEQ ID NO: 20; see the attached sequence alignment.

The examiner suggests changing the language of the claim to: "An oligonucleotide probe consisting of a nucleotide sequence etc".

4. Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka, Ph.D., whose telephone number is (703) 305-7270. The examiner can normally be reached Monday-Friday from 10:00 a.m. to 4:30 p.m.

If attempts to reach examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, Ph.D. can be reached on (703) 308-3804. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionists whose telephone number is (703) 308-0196.

Malgorzata A. Walicka, Ph.D.

Patent Examiner

Art Unit 1652

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